

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application No.:	09/859,701	:	Examiner:	Davis, Deborah A.
Filed:	May 16, 2001	:	TC/A U:	1655
Applicant:	Warner, Benjamin P.	:	Confirmation No.:	4132
Docket No.:	60184.24	:	Customer No.:	27128
Title:	METHOD FOR DETECTING BINDING EVENTS USING MICRO-X-RAY FLUORESCENCE SPECTROMETRY			

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*Via EFS-Web*

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

**DECLARATION OF BENJAMIN P. WARNER**  
**PURSUANT TO 37 C.F.R. § 1.132**

1. I am an inventor of the above-identified U.S. patent application.
2. I have been the Chief Executive Officer of Caldera Pharmaceuticals, Inc., a spinoff of Los Alamos National Laboratory, since September 2005. Immediately prior to my present employment, I was a Scientist with Los Alamos National Laboratory, based in Los Alamos, New Mexico, from 1995-2005. I was the Project Leader for Los Alamos National Laboratory's National Security, Chemistry Division from 2000-2005. My primary areas of research include biomedical technology; counter-terrorism technology; dosimetry technology; counter-chemical weapon defense applications; high-throughput, small molecule measurement technology; and electro-optic devices.
3. I received a Ph.D. in Chemistry from Massachusetts Institute of Technology (MIT) in 1995. While at MIT, my research included organic synthesis; molecular recognition;

molecular devices; and biomimetic chemistry. I received a B.S. in Chemistry from The University of the South.

4. Selected publications of mine include:

- (i) MESA: Measurement of Enzyme-Substrate Affinities. B. Warner, E. Minogue, and G. Havrilla; 2005 R&D 100 Winner, R&D Magazine, September 2005;
- (ii) A high throughput screening method for the selection of zeolites for binding cations. E. Minogue et al.; Chemical Communications, 2005, 4167-4168;
- (iii) Micro-X-ray fluorescence as a general high-throughput screening method for catalyst discovery and small molecule recognition. T. Miller, G. Mann, G. Havrilla, C. Wells, B. Warner, and R. Baker; Journal Of Combinatorial Chemistry, 2003, 5, 245; and
- (iv) Controlled Acceleration and Inhibition of the Bergman Cyclization. B. Warner, S. Millar, R. Broene, and S. Buchwald; Science, 1995, 269, 814.

5. I have reviewed International Publication No. WO 90/15070 to Pirrung et al. and U.S. Patent No. 4,436,826 to Wang that have been cited by the U.S. Patent and Trademark Office as a basis for rejecting my invention as being obvious. I have compared the Pirrung and Wang references to my invention as disclosed and now claimed in the present patent application. After reviewing the Pirrung and Wang references, it is my firm conviction that these references do not render my invention obvious.

6. My invention is a method for detecting a binding event between members of a surface-bound receptor array and at least one potential binder using micro-x-ray fluorescence spectroscopy. My invention uses X-ray fluorescence as a probe to detect binding events between receptors and potential binders. In particular, my invention includes a method for detecting a

binding event between at least one binder and members of a receptor array. The receptors are exposed to at least one binder and then arrayed on a substrate. The array is then exposed to X-ray radiation and an X-ray fluorescent signal from any bound member of the array is detected and used to determine where a binding event has occurred.

7. The combination of the Pirrung and Wang references does not yield my invention for at least three reasons:

- (i) First, Pirrung and Wang both require radioactive or fluorescent tags or labels to measure the sample whereas my invention uses at least one untagged component.
- (ii) In Wang, it is the fluorescent tag that is the source of the X-ray fluorescence signal. Without a tag, Wang would not be able to detect the XRF signal. In my invention, the XRF signal specifically comes from the bound member(s) of the array and not from a tag.
- (iii) Wang uses tags that are “unassociated chemically” with the component being analyzed. In order to be “unassociated chemically,” Wang encloses the tag in latex or a similar coating. In contrast, my invention measures element that are chemically associated and that are intrinsically integral to the component being measured.

8. Accordingly, it is my opinion after reviewing the Pirrung and Wang references that these references do not render my invention obvious.

9. I declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful, false statements and the like are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and such willful, false statements may jeopardize the validity of any patents issued from the patent application.

Respectfully submitted,



Date: 18 October 2007

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Benjamin P. Warner, Ph.D.